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Prism adaptation reverses the local processing bias in patients with right temporo-parietal junction lesions

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Lesions to the right temporo-parietal cortex commonly result in hemispatial neglect. Lesions to the same area are also associated with hyperattention to local details of a scene and difficulty perceiving the global structure. This local processing bias is an important factor contributing to neglect and may contribute to the higher prevalence of the disorder following right compared with left hemisphere strokes. In recent years, visuomotor adaptation to rightward-shifting prisms has been introduced as a promising treatment for hemispatial neglect. Explanations for these improvements have generally described a leftward realignment of attention, however, the present investigation provides evidence that prism adaptation reduces the local processing bias. Five patients with right temporal-parietal junction lesions were asked to identify the global or local levels of hierarchical figures before and after visuomotor adaptation to rightward-shifting prisms. Prior to prism adaptation the patients had difficulty ignoring the local elements when identifying the global component. Following prism adaptation, however, this pattern was reversed, with greater global interference during local level identification. The results suggest that prism adaptation may improve non-spatially lateralized deficits that contribute to the neglect syndrome.

Keywords: hemispatial neglect; visual attention; prism adaptation; hierarchical processing

Introduction

Lesions to the right temporo-parietal cortex commonly result in hemispatial neglect (‘neglect’), a disorder in which patients show difficulty responding or orienting to objects and events that appear on the left side of space (Friedrich *et al*., 1998; Karnath *et al*., 2003). Even patients with chronic temporal-parietal junction lesions whose neglect has recovered can have persistent subclinical deficits in directing attention to the left side (Eglin *et al*., 1989) and disengaging attention away from right-sided stimuli (Posner *et al*., 1984).

Right temporo-parietal junction lesions are also associated with hyperattention to local details of a scene and difficulty perceiving the global structure. Right hemisphere damage was first associated with global processing deficits by Delis and colleagues (1986) who asked patients with unilateral lesions to copy pictures in which identical smaller components are arranged to form larger shapes (so-called ‘hierarchical’ figures, e.g. a large A built out of small S’s; Fig. 1). Patients with large right hemisphere lesions such as those that lead to neglect tended to draw many copies of the local element in a disorganized arrangement, failing to reproduce the global structure. Similarly, Marshall and Halligan (1995)

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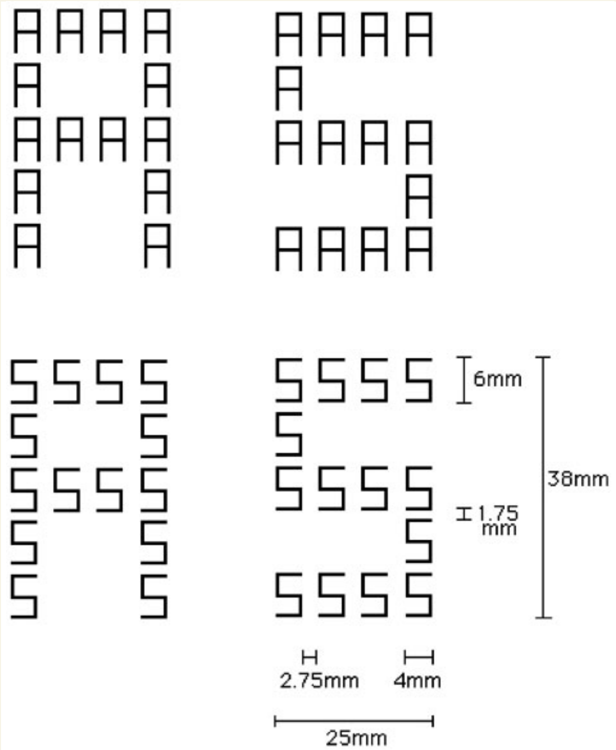

Figure 1 Experimental stimuli, based on Navon (1977).

reported a patient with a large right hemisphere lesion who was able to identify the global form of hierarchical stimuli but when instructed to cross out all the local elements only crossed out targets on the right side of the stimuli, suggesting that she could not sustain a representation of the global form. This local processing bias—or global processing deficit—was localized to the right temporo-parietal junction through a series of reaction time studies involving patients with different focal lesions, with left temporo-parietal junction lesions resulting in a local processing deficit (Robertson *et al*., 1988).

Although the local processing bias is not uniquely observed in patients with neglect, it is an important factor contributing to the disorder and may be one reason for the higher prevalence of neglect following right compared with left hemisphere damage (Rafal and Robertson, 1995). Patients can get locked onto small parts of the scene and fail entirely to perceive the critical big picture. Neglect severity is reduced under conditions that encourage the patients to deploy their attention more globally. For example, bisection bias is smaller when the to-be-bisected stimulus is a square rather than a line, probably because the rightward vertical side of the square enhances the right hemisphere's global processing capacity (Halligan and Marshall, 1994). Similarly, performance is improved under conditions that reduce the number of local elements available to capture attention. Line cancellation performance is better when patients erase lines, eliminating the capture of attention by right-sided detail, than when they draw over them (Mark *et al*., 1988). When a neglect patient was asked to place numbers on a clock face with all numbers on a single dial she showed the classic pattern of compressing all numbers to the right side, but she had accurate number placement with no spatial bias when instructed to place each number on a separate dial (di Pellegrino, 1995). Ishai and colleagues (1996) found that neglect patients could correctly discriminate between complete and incomplete pictures of daisies, but omitted left-sided detail when performing the more attentionally demanding task of copying complete daisies. These studies suggest that the capture of attention to right-sided local detail contributes to the severity of neglect.

Over the past decade, promising evidence has emerged for the amelioration of neglect following visuo-motor adaptation to rightward prismatic shifts in the visual field. Rossetti and colleagues (1998) asked neglect patients to make 50 pointing movements to visual targets while wearing goggles fitted with neutral lenses (control group) or prisms that induced a 10° rightward shift in the visual field (treatment group). After prism adaptation the treatment group showed the same leftward pointing bias in their adapted arm that is observed in healthy participants, but more importantly there were also improvements in neglect symptoms as measured by standard pen-and-paper tests.

Subsequent research has shown that the benefits of prism adaptation generalize to a wide range of performance measures, including tests of visual perception (Farnè *et al*., 2002; Pisella *et al*., 2002; Berberovic *et al*., 2004), tactile perception (Maravita *et al*., 2003), somatosensation (Dijkerman *et al*., 2004), haptic exploration (McIntosh *et al*., 2002), postural stability (Tilikete *et al*., 2001) and wheelchair navigation (Jacquin-Courtois *et al*., 2008), although no prism effects were observed on patients' perceptions of chimeric faces (Ferber *et al*., 2003), relative size judgements of bilaterally presented objects (Dijkerman *et al*., 2003) or visual search performance (Morris *et al*., 2005). The benefits of a single 5-min session of prism adaptation are frequently found to last at least 2 h (Rossetti *et al*., 1998; Rode *et al*., 2001) and for as much as 24 h (Rode *et al*., 2001; Farnè *et al*., 2002; Pisella *et al*., 2002) or even 1-week post-treatment (Dijkerman *et al*., 2004). Overall, evidence from many studies suggests that prism adaptation is a brief and simple treatment that results in relatively long-lasting improvements across a broad range of neglect symptoms.

Explanations for the clinical benefits induced by prism adaptation have generally described a leftward realignment of attention, for example through a resetting of the ocular-motor system (Serino *et al*., 2006). The present research investigates another possibility: that adaptation to rightward-shifting prisms could improve neglect symptoms by alleviating the local processing bias. Five patients selected on the basis of right temporo-parietal junction lesions were tested on a directed attention task before and after prism adaptation. In separate blocks patients identified the global or local levels of hierarchical stimuli in which large S's and A's were formed out of small S's or A's (Fig. 1). The stimuli could be congruent (e.g. a large S built of small S's) or incongruent (e.g. a large S built of small A's). This hierarchical processing task, first used by Navon (1977), allows measurement of the extent to which participants are able to ignore the information on one level while directing their attention to another. Navon found that healthy participants have difficulty inhibiting their processing of the global form, with slower responses for incongruent compared with congruent stimuli in the local block. In contrast, he found that interference of the local form during the global block was absent indicating the relative superiority of global processing in healthy participants.

It was predicted that, before prism adaptation, patients would show deficits in ignoring the local stimuli when identifying global forms relative to their ability to ignore global stimuli when identifying local forms. If adaptation to rightward-shifting prisms reduces the local processing bias then this would be reflected by significantly smaller local interference (LI) and/or greater global interference (GI) after prism adaptation.

Methods

Participants

Patients

Five patients (mean age = 56.8 years, SEM = 4.68) with chronic lesions to the right temporo-parietal junction and intact visual fields were recruited and gave informed consent to participate in a research protocol approved by hospital and university ethic committees according to the Declaration of Helsinki. The clinical details of these patients are shown in Table 1 and their lesion locations are shown in the Supplementary figure. Three patients (A.C., G.S. and N.B.) showed visual extinction on neurological confrontation testing. Patients G.S. and J.D. had previously suffered from neglect, which had resolved by the time of testing. One patient, A.C., showed neglect at the time of testing based on the results of standard pen-and-paper tests (Supplementary table). This patient had also shown anosagnosia for his hemiplegia in the weeks immediately following his stroke, and some anosodiaphoria remained at the time of the present study. In addition to the main experimental task, he completed three pen-and-paper tests for neglect (Wilson *et al*., 1987) and showed improved performance only on the line bisection task (pre-adaptation: 14.6% versus post-adaptation 0.3% rightwards error).

Control participants

Ten age- and gender-matched control participants were tested on the hierarchical processing task to provide a baseline with which to compare the pre- and post-adaptation performance of the patients. The control group had a mean age of 56.2 years (SEM = 3.0), and scored an average of –0.88 (SEM = 0.05) on the Edinburgh Handedness Inventory (where –1 denotes extreme right-handedness and +1 denotes extreme left handedness; Oldfield, 1971).

Stimuli and procedure

The patients completed the following sequence of tasks: (i) pre-adaptation hierarchical processing; (ii) pre-adaptation open-loop pointing; (iii) prism adaptation; (iv) post-adaptation open-loop pointing; and (v) post-adaptation hierarchical processing. The control participants completed the hierarchical processing task only.

(i) Pre-adaptation hierarchical processing

A hierarchical processing task was designed based on the results of a pilot study with twelve healthy older participants so that approximately equal reaction times and interference effects were obtained for global and local stimuli. Stimuli were presented on a computer screen positioned 60 cm from the participant's eyes. Each participant identified the global or local levels of hierarchical stimuli in two separate blocks ('globally directed' and 'locally directed'), with practice provided prior to each block as required. The order of events for each trial is shown in Fig. 2. The trial began with a 500-Hz tone presented for 500 ms. After a further delay of 100 ms a 3-mm × 3-mm central fixation cross appeared. Participants were instructed to look at the cross throughout the entire trial. After 500 ms the fixation cross was joined by a hierarchical stimulus (Fig. 1) presented in the left or right visual field such that there was 2.4 mm between the fixation cross edge and the inner edge of the hierarchical stimulus. The stimuli consisted of eleven small 4-mm wide 6-mm high S's and A's (the local forms) arranged to form large 25-mm wide × 38-mm high S's and A's (the global form). The identity of the local and global forms could be identical (congruent) or different (incongruent), resulting in four stimuli. There were 16 repetitions of each of the four stimuli within each visual field, with a total of 128 trials per global and local block. These were presented in one block per condition for all patients (counterbalanced between patients) except A.C., who completed two global and two local blocks of 64 trials per block before and after prism adaptation in local-global-global-local (LGGL) order.

The stimulus remained on the screen for 500 ms for patient A.C. and 200 ms for all other participants, after which time it was replaced by a blank screen. In the locally directed block the participants identified the local feature. In the globally directed block the participants identified the global form. Participants indicated their decision (S or A) by pressing one of two buttons on a standard mouse with the index and middle fingers of their right hand (that is, the patients' ipsilesional hand). Button assignment was counterbalanced between participants, who practiced the response mapping prior to the commencement of the experiment. The participants were instructed to respond as quickly and as accurately as possible. The participant's response ended the trial, with a timeout after 3000 ms. There was an inter-trial interval of 1000 ms.

Table 1 **Clinical details of the patients who participated in the study**

Patient	Age	Sex	Type of stroke	Weeks since stoke	Handedness	Limb weakness[a]	Visual extinction[a]	Visual neglect[a]
A.C.	72	M	Ischaemic	47	R	b	b	b
G.S.	62	M	Ischaemic	111	L	b	b	c
N.B.	55	M	Subarr. Haem.	252	R		b	
J.D.	49	F	Ischaemic	181	R	c	c	c
D.B.	46	M	Ischaemic	31	R	c		

a Based on standard neurological examination.
b Present at time of testing.
c Previously present but resolved.

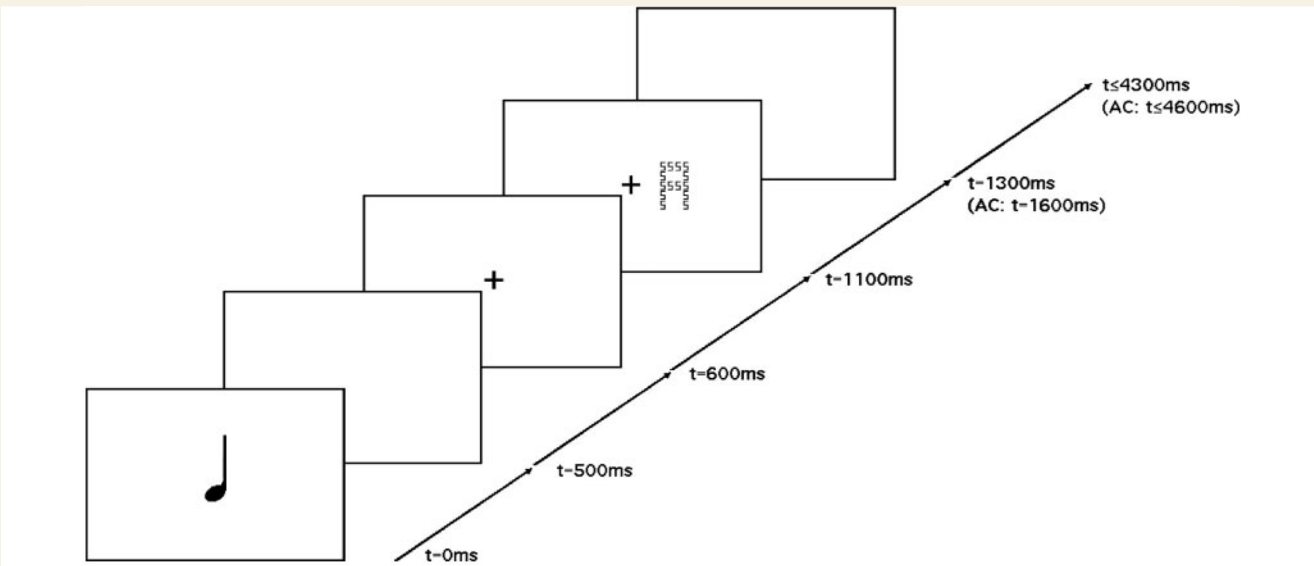

Figure 2 The timecourse of events for the hierarchical processing task.

(ii) Pre-adaptation open-loop pointing

The patients' open-loop pointing errors were measured with the aid of a semi-circular panel (radius = 59 cm) that occluded their pointing arm from their vision. Three target lines were drawn on the upper surface of the panel radiating out at –10°, 0° and +10° from the patient's body midline. The panel was held under the patient's chin while they pointed their arm under each of the target lines four times in pseudo-random order, returning their hand to rest in front of their torso between each pointing movement. Pointing error was measured by the experimenter to the nearest 0.5° with the aid of markings drawn on the underside of the panel. Leftward errors were recorded as negative numbers and rightward errors were recorded as positive numbers.

(iii) Prism adaptation

The panel was removed and the patients were fitted with prism glasses that had been constructed by inserting two adjustable Risley biprisms into optician's trial frames. These were set to induce a 15° rightward shift for all patients. The patients pointed alternately with their right hand to visual targets held at eye level and arm's length 10° to the left and right of body midline. The construction of the prism glasses was such that the first half of the patient's pointing movement was occluded from their view. They made 50 pointing movements as fast as possible, returning their hand to their torso in between each pointing movement.

(iv) Post-adaptation open-loop pointing

To confirm adaptation an open-loop pointing session was conducted immediately after prism adaptation using the same procedure as described above in (ii) for the pre-adaptation open-loop pointing.

(v) Post-adaptation hierarchical processing

Patients completed the global and local processing tasks using the same procedure as described in (i), above.

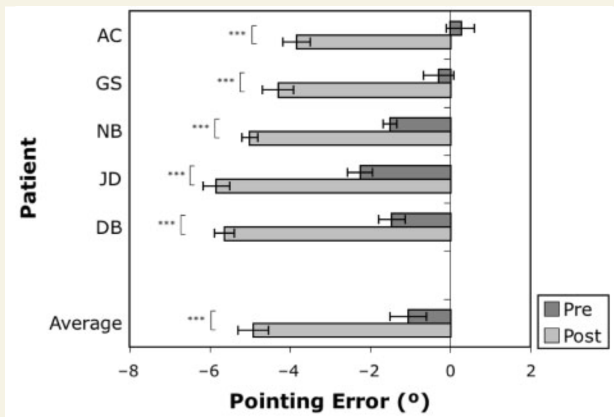

Figure 3 Pointing errors of the individual patients before and after prism adaptation. Error bars represent one SEM; ***indicates $P < 0.001$.

Results

Prism adaptation

The control participants were not tested with prisms and therefore no adaptation was measured. In the patients, paired-samples *t*-tests performed on the raw pointing errors for each individual confirmed that they each showed significant leftward after-effects ($P < 0.001$; Fig. 3). The average shift magnitude was 4.08°.

Hierarchical processing

Analysis of response rates

The healthy controls showed a 99% response rate, of which 96% were accurate. The response rates and accuracy of patients

N.B., G.S., J.D. and D.B. were also at ceiling, with an average of 96% of trials responded to and with 94% accuracy. Such low error rates precluded meaningful analyses.

Because A.C. showed a dramatically different pattern of errors, these were analysed separately. A.C. had a lower response rate (59% of all trials) and accuracy rate (87% of responded-to trials). Many more of his accurate responses were in the right visual field (83% of all right visual field trials) than left visual field (19% of all left visual field trials). His response rates were therefore pooled over visual field for further analysis. A.C.'s accuracy was at ceiling for the congruent trials (>95% of responded-to trials), however, chi-squared analyses were performed to determine whether his accuracy for incongruent trials in the globally and locally directed task changed as a result of prism adaptation. Accuracy for incongruent trials in the locally directed task before adaptation was at ceiling (97.5%), precluding statistical analysis, but it is of note that this dropped to 89.4% following prism adaptation, consistent with increased interference of the global form. In contrast, there was a significant increase in accuracy for incongruent trials in the globally directed task from 43.2% to 77.1% following prism adaptation ($\chi^2 = 8.59$, $P < 0.005$), consistent with decreased interference of the local information.

Analysis of reaction times

Preliminary analysis for visual field effects

As A.C. responded to only 19% of left visual field stimuli a preliminary session (pre, post) × Visual Field (left, right) × Level (global, local) × Congruency (congruent, incongruent) was performed on the data from the four other patients to examine for any visual field effects. Although inspection of individual patient data reveal a general pattern of right visual field advantage (Table 2), there were no main effects or interactions involving Visual Field ($P > 0.05$), therefore data were collapsed across visual fields for both the control and patient group analyses.

Control participants

The mean reaction times for the control participants are shown in Table 3. A two-way repeated measures ANOVA was performed with Level (global, local) and Congruency (congruent, incongruent) as within-subjects factors. There was a 43 ms main effect of congruency [$F(1, 9) = 22.9$, $P < 0.001$], with significantly faster responses for congruent ($M = 631.8$, SEM = 31.3) than incongruent ($M = 674.5$, SEM = 28.0) stimuli. The reaction time cost for incongruent compared to congruent stimuli was larger for the locally directed task (49 ms) than the globally directed task (36 ms), however, this difference was not significant [$t(9) = 0.568$, $P = 0.584$]. There were no further significant main effects or interactions ($P > 0.05$).

Patients

The reaction times for the pre- and post-adaptation performance of the patient group are shown in Tables 4 and 5. Interference of

Table 2 Patient reaction times for the left and right visual field across session

Patient	Pre-adaptation			Post-adaptation		
	LVF	RVF	RVF–LVF	LVF	RVF	RVF–LVF
G.S.	876	796	80	920	797	123
N.B.	742	827	−84	694	795	−101
J.D.	762	723	39	747	725	22
D.B.	897	885	12	851	812	40
Mean	819	808	12	803	782	21

No data are provided for patient A.C. due to his low response rate to left visual field stimuli (19%).
LVF = left visual field, RVF = right visual field.

Table 3 Control reaction times for the global and local processing tasks

	Global target			Local target		
	Congruent	Incongruent	LI	Congruent	Incongruent	GI
C1	586	672	86	537	586	50
C2	532	621	89	545	598	53
C3	796	819	23	743	774	31
C4	745	762	17	670	803	133
C5	575	688	113	454	440	−13
C6	679	649	−31	854	865	11
C7	531	523	−8	690	709	19
C8	585	624	39	576	616	39
C9	543	585	42	557	630	73
C10	648	641	−7	793	887	94
Mean	622	658	36	642	691	49

Table 4 Patient reaction times for the pre-adaptation global and local processing tasks

	Global target			Local target		
	Congruent	Incongruent	LI	Congruent	Incongruent	GI
A.C.	994	1128	134	969	1013	45
G.S.	859	937	78	728	746	18
N.B.	714	849	135	788	791	3
J.D.	712	762	50	710	786	75
D.B.	639	669	30	1214	1282	68
Mean	784	869	85	882	924	42

Table 5 Patient reaction times for the post-adaptation global and local processing tasks

	Global target			Local target		
	Congruent	Incongruent	LI	Congruent	Incongruent	GI
A.C.	1111	1260	149	874	1105	231
G.S.	916	945	28	746	788	43
N.B.	732	740	8	727	772	46
J.D.	704	748	43	695	798	103
D.B.	626	634	7	1000	1122	122
Mean	818	865	47	808	917	109

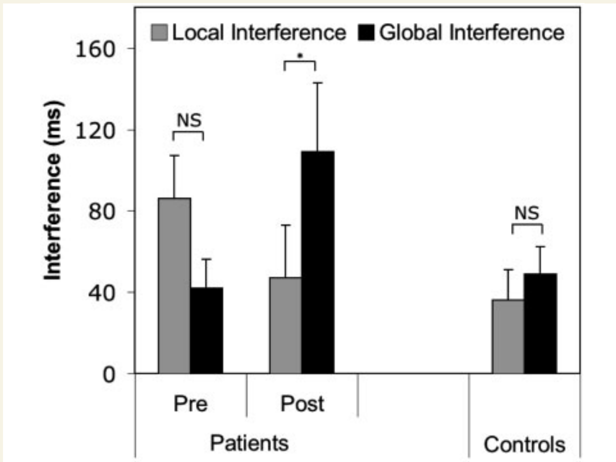

Figure 4 GI and LI for patients before and after prism adaptation and age-matched controls. Error bars represent +1 SEM; *indicates $P<0.05$; NS indicates $P>0.05$.

each level was also calculated as the difference between congruent and incongruent reaction times: LI was calculated as the effect of task-irrelevant incongruent local information when identifying global targets, whereas GI was calculated as the effect of task-irrelevant incongruent global information when identifying local targets. A three-way repeated-measures ANOVA of mean reaction times was performed with Session (pre, post), Level (global, local) and Congruency (congruent, incongruent) as within-subjects factors. There was a significant main effect of Congruency [81 ms, $F(1, 4)=15.8$, $P<0.05$], reflecting faster responses for congruent stimuli ($M=822.9$, SEM = 49.9) than incongruent stimuli ($M=893.7$, SEM = 64.3). No other main effects were significant ($P>0.05$).

The important finding for the purposes of this study, however, was a significant Session × Level × Congruency interaction [$F(1,4)=14.5$, $P<0.05$]. This interaction reflects that the amount of GI and LI changed after prism adaptation (Fig. 4). *A priori* *t*-tests were used to examine GI and LI before and after prism adaptation. Prior to prism adaptation there was significant LI in the globally directed task, with responses 85 ms faster for congruent stimuli ($M=783.6$, SEM = 63.6) than incongruent stimuli ($M=868.9$, SEM = 78.6); $t(4)=4.00$, $P<0.05$. There was also significant GI on responses in the locally directed task, with responses 42 ms faster for congruent stimuli ($M=881.8$, SEM = 94.8) than incongruent stimuli ($M=923.6$, SEM = 101.1); $t(4)=3.00$, $P<0.05$. The reaction time cost of incongruent compared with congruent global information in the locally directed task was more than twice the interference effect in the globally directed task, although a *t*-test comparing these interference effects was not significant [$t(4)=1.33$, $P=0.25$].

This pattern was reversed following prism adaptation. The pre-adaptation 85 ms LI effect decreased to 47 ms and was not significant: congruent ($M=818.2$, SEM = 87.4) compared with incongruent ($M=865.3$, SEM = 110.8); $t(4)=1.79$, $P=0.149$. In comparison, the pre-adaptation 42 ms GI effect reliably increased to 109 ms: congruent ($M=808.3$, SEM = 56.9) compared with incongruent ($M=917.1$, SEM = 80.3); $t(4)=3.17$, $P<0.05$.

Table 6 LI-to-GI ratios for each patient

Patient	Pre-adaptation	Post-adaptation
A.C.	3.02	0.65
G.S.	4.40	0.66
N.B.	44.34	0.17
J.D.	0.66	0.42
D.B.	0.45	0.06
Average	10.57	0.39
Controls	95% CI $= -2.79 \leqslant \bar{X} \leqslant 1.59$	

Post-adaptation, the GI in the locally directed task was also significantly larger than the LI in the globally directed task [$t(4)=3.58$, $P<0.05$]. In summary, the analysis revealed that following prism adaptation there was an increase in GI in the locally directed task and a reciprocal decrease in LI in the globally directed task. No other interactions reached significance (P>0.05).

Comparison of the control participants and patients

This investigation was motivated by the hypothesis that reduced global processing and exaggerated LI in patients with right temporo-parietal junction lesions would be reduced by prism adaptation. To assess the effects of prism adaptation on the balance between global and local processing, LI-to-GI ratios were calculated for the pre- and post-adaptation performance of each patient and each control participant. These were computed as the ratio LI/GI, where a value of 1 indicates equivalent LI and GI.

The interference ratios for each patient were compared to the 95% CI constructed around the control group ratios (Table 6). As a group, the patients' mean ratio was 10.57 in the pre-adaptation phase, whereas it decreased to 0.39 in the post-adaptation phase. The mean for the control group was –0.60, with the 95% CI ranging from –2.79 to 1.59. Prior to prism adaptation A.C., G.S. and N.B. showed LI-to-GI ratios that were outside the upper boundary of the 95% CI around the control mean. This indicates that LI was significantly larger than GI for these three participants compared to controls. After prism adaptation, however, the LI-to-GI ratios for these three patients were within normal range. The interference ratios for patients J.D. and D.B. also decreased after prism adaptation, but were within normal range in both sessions.

Discussion

In a hierarchical processing task, healthy older controls showed similar levels of GI and LI. When this same task was presented to five patients with right temporo-parietal junction lesions before and after rightward prism adaptation, the results demonstrate a reduction in their local processing bias. Prior to prism adaptation, the patients had greater LI than GI as a group, and individually three of these patients showed LI-to-GI ratios that differed significantly from the age-matched controls. This is consistent with previous literature linking right temporo-parietal junction lesions with deficits in filtering out and disengaging from local detail in comparison with the global form. This pattern reversed following prism adaptation: as a group the patients showed greater GI than LI and individually none of the five patients had LI-to-GI ratios that were different from controls'.

Although no sham treatment condition was used, it is unlikely that a placebo would induce such specific, reciprocal changes in LI and GI. Similarly, the consistency of the changes across the five individual patients suggests that the observed improvement was not the product of spontaneous performance fluctuations.

Furthermore, these changes in hierarchical processing occurred without a concomitant change in spatially lateralized attention; no reliable effects of prism adaptation on visual field were found. This is most likely because the patients, who were selected on the basis of lesion location and not behavioural performance, did not show a robust right visual field bias before prism adaptation. Importantly, it highlights the possibility that prism adaptation affects more than just spatially lateralized functions.

One interpretation is that the greater LI prior to prism adaptation was due to a lateralized bias in the allocation of attention within each stimulus, which interfered with perception of the global level. In this case the changes in interference effects after prism adaptation would be explained by improvement in the lateralized object-based allocation of attention rather than modification of hierarchical processing *per se*. Two points militate against this possibility. First, responses to global targets were faster than to local targets in both sessions, which is the contrary to the pattern predicted by a lateralized bias selectively impairing global identification. Second, both target letters (S and A) are readily discriminable based on right-sided information alone. For these reasons, the data are better explained by modified hierarchical processing following prism adaptation.

Research into the rehabilitation of neglect is a high priority as the disorder is associated with poor functional outcome and decreased independence (Jehkonen *et al*., 2006). Unfortunately it has proven difficult to identify an intervention that is brief and simple enough to administer to stroke patients, that provides long-lasting benefits, and which generates improvements that generalize to activities outside the treatment setting (see Luauté *et al*., 2006*a*, for a review of treatment methods). A single session of prism adaptation can ameliorate a wide range of sensory and cognitive manifestations of spatial neglect for as much as 1-week post-treatment. Evidence from two longitudinal studies show that these improvements can be sustained for as much as 5 weeks (Frassinetti *et al*., 2002) or even 6 months (Serino *et al*., 2007) following a 2-week programme of *repeated* adaptation sessions. The existing literature therefore suggests that prism adaptation is a promising treatment for neglect.

Although the defining symptom of neglect is difficulty attending to the contralesional hemispace, there are a number of other deficits associated with neglect that are not more pronounced on one side of space than the other. These 'non-spatially lateralized' deficits include impaired sustained attention (Robertson *et al*., 1997), impaired spatial working memory (Husain *et al*., 2001), and hyperattention to local detail in preference to global scenes—the local processing bias (Marshall and Halligan, 1995). Although these non-spatially lateralized deficits are not necessarily specific to neglect, they may increase neglect severity and reduce the potential for recovery (Husain and Rorden, 2003). For example, neglect patients with sustained attention deficits are less likely to recover than those without (Samuelsson *et al*., 1998), and vigilance training aimed at improving sustained attention also benefits neglect symptoms (Robertson *et al*., 1995). It is perhaps worth noting that in the present study the three patients who showed significant local processing biases before prism adaptation were also the only three who had clinical signs of hemi-inattention at the time of testing.

Rode and colleagues (2006*b*) reported the case of a neglect patient who showed improved spatial dysgraphia following adaptation to rightward-shifting prisms. Improvements were observed in both spatially lateralized and non-lateralized symptoms: there was a reduction in the patient's tendency to restrict writing to the right side of the page as well as in the degree of visuo-constructional abnormalities such as exaggerated word spacing, graphic errors and line sloping. Similar improvements in neglect and constructional apraxia were reported in two patients who copied complex figures before and after prism adaptation (Rode *et al*., 2006*a*). The amelioration of non-lateralized deficits such as constructional apraxia and the local processing bias by prism adaptation may explain why the technique appears to be more successful than many other treatment methods.

It is of interest to consider the neurological process through which prism adaptation may improve both hemispatial neglect and the local processing bias. One explanation is that it may restore the balance of activation levels between the two cerebral hemispheres. Kinsbourne (1970, 1993) argued that the left and right hemispheres direct attention contralaterally in a mutually opponent fashion. Damage to the right hemisphere results in disinhibition of left hemisphere function; hence neglect can also be considered to be a hyperattention to the right hemispace rather than impaired leftward attention. Similarly, right hemisphere damage leads to impaired global processing but also hyperattention to local detail as a result of left hemisphere disinhibition.

Restoring the balance of activity between the two hemispheres by increasing right hemisphere activation improves neglect symptoms. For example, performance on a cancellation task improves if patients simultaneously make small repetitive movements with their left hand (Robertson and North, 1992). Bilateral hand movements result in no benefits to neglect symptoms (Robertson and North, 1994), suggesting that the activation of the damaged right hemisphere relative to the left is the restorative factor. Limb activation therapy, in which patients are trained to move their contralesional arm at regular intervals, is a treatment based on these findings (Robertson *et al*., 1998). Improvements in left inattention can even be observed when left limb movement is merely implied rather than actually performed: activation of the right hemisphere by presenting an object in the display that affords action by the left hand—a teacup with a handle pointing to the left—also reduced visual extinction, even though the teacup and the direction of its handle were irrelevant to the task (di Pellegrino *et al*., 2005). Finally, when repetitive transcranial magnetic stimulation (rTMS) is applied over the left hemisphere, inhibiting activity in the stimulated areas, neglect symptoms improve in patients with right hemisphere lesions (Fierro *et al*., 2006; Shindo *et al*., 2006).

Changes in relative hemispheric activity have already been proposed as a mechanism for the clinical effects of prism adaptation by Pisella and colleagues (2006). They put forward a hypothesis, based partially on their studies of visuo-motor adaptation in patients with lesions to the cerebellum (Pisella *et al*., 2005) and the parietal lobe bilaterally (Pisella *et al*., 2004; see also Newport and Jackson, 2006) that visual error signals caused during prism exposure lead to the generation of a bottom-up signal in the right cerebellum that is transferred via a network of left and right hemisphere areas to ultimately modify activity in the left parietal lobe. They suggest that this may lead to the recruitment of left hemisphere areas for functions that would usually be served by the damaged right hemisphere, however their model could just as easily provide for a reduction in left hemisphere activity, reducing the inhibition of residual right hemisphere function. Support for this explanation is provided by Luauté and colleagues (2006b), who found reduced activity in the left posterior parietal cortex of neglect patients who had undergone prism adaptation which correlated with improved performance on a standard neglect battery (Wilson *et al*., 1987). Reduction of left posterior parietal cortex activity by adaptation to rightward-shifting prisms could improve both the leftward inattention and the local processing bias by restoring the activation balance of the two hemispheres.

There is now substantial evidence that prism adaptation improves the spatial attention bias of neglect as manifested on a wide range of tests. The results from the present study suggest that a promising avenue for future investigation could be to examine the effects of prism adaptation on non-spatially lateralized deficits other than the local processing bias. If prism adaptation also ameliorates a wide range of non-spatially lateralized symptoms in addition to the spatial attention deficit of neglect then this may explain its greater effectiveness compared to other treatment methods.

Supplementary material

Supplementary material is available at *Brain* online.

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